? ds

Set	Items	Description
S1	1563	UTERUS
S2	4532	CERVI?
S3	475	S1 AND S2
S4	41	CARCINOSARCOMA
S5	9	S3 AND S4
S6	590	CERVI?(5N)UTER?
S7	22954	CANCER
S8	224	S6 AND S7
S9	41	CARCINOSARCOMA

? s s8 and s9

	224	S8
	41	S9
S10	5	S8 AND S9

? t s10/3,k,ab/1-5

10/3,K,AB/1

DIALOG(R)File 340:CLAIMS(R)/US Patent

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IFI Chemical Acc No: 2004-0035590
Document Type: C

METHOD OF USING A COX-2 INHIBITOR AND A TACE INHIBITORS AS A COMBINATION THERAPY

Inventors: Masferrer Jaime L (US); Stephenson Diane T (US)
Assignee: Pharmacia Corp
Assignee Code: 63809
Publication (No,Kind,Date), Applic (No,Date):
US 20040122011 A1 20040624 US 2003423526 20030425
Priority Applic(No,Date): US 2003423526 20030425; US 99470951 19991222; US 2001868063 20011005
Provisional Applic(No,Date): US 60-113786 19981223

Abstract: The present invention provides compositions and methods to treat, prevent or inhibit a neoplasia, a neoplasia-related disorder, pain, inflammation, an inflammatory-related disorder, a vasoocclusive event or a vaso-occlusive-related disorder in a mammal using a combination of a COX-2 inhibitor and a TACE inhibitor.

Non-exemplary Claims: ...lymphocytic leukemia, acute myeloid leukemia, adenocarcinoma, adenoid cycstic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, anal canal **cancer** , anal **cancer** , anorectum **cancer** , astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, biliary **cancer** , bone **cancer** , bone marrow **cancer** , brain **cancer** , breast **cancer** , bronchial **cancer** , bronchial gland carcinomas, carcinoids, carcinoma, **carcinosarcoma** , cholangiocarcinoma, chondosarcoma, choriod plexus papilloma/carcinoma, chronic lymphocytic leukemia, chronic myeloid leukemia, clear cell carcinoma, colon **cancer** , colorectal **cancer** , connective tissue **cancer** , cystadenoma, digestive system **cancer** , duodenum **cancer** , endocrine system **cancer** , endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, endothelial cell **cancer** , ependymal **cancer** , epithelial cell **cancer** , esophageal **cancer** , Ewing's sarcoma, eye and orbit **cancer** , female genital **cancer** , focal nodular hyperplasia, gallbladder **cancer** , gastric antrum **cancer** , gastric fundus **cancer** , gastrinoma, germ cell tumors, glioblastoma, glucagonoma, heart **cancer** , hemangiblastomas, hemangioendothelioma,

hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatobiliary **cancer** , hepatocellular carcinoma, Hodgkin's disease, ileum **cancer** , insulinoma, intaepithelial neoplasia, interepithelial squamous cell neoplasia, intrahepatic bile duct **cancer** , invasive squamous cell carcinoma, jejunum **cancer** , joint **cancer** , Kaposi's sarcoma, kidney and renal pelvic **cancer** , large cell carcinoma, large intestine **cancer** , larynx **cancer** , leiomyosarcoma, lentigo maligna melanomas, leukemia, liver **cancer** , lung **cancer** , lymphoma, male genital **cancer** , malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal **cancer** , mesothelial **cancer** , metastatic carcinoma, mouth **cancer** , mucoepidermoid carcinoma, multiple myeloma, muscle **cancer** , nasal tract **cancer** , nervous system **cancer** , neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, non-epithelial skin **cancer** , non-Hodgkin's lymphoma, oat cell carcinoma, oligodendroglial **cancer** , oral cavity **cancer** , osteosarcoma, ovarian **cancer** , pancreatic **cancer** , papillary serous adenocarcinoma, penile **cancer** , pharynx **cancer** , pituitary tumors, plasmacytoma, prostate **cancer** , pseudosarcoma, pulmonary blastoma, rectal **cancer** , renal cell carcinoma, respiratory system **cancer** , retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, sinus **cancer** , skin **cancer** , small cell carcinoma, small intestine **cancer** , smooth muscle **cancer** , soft tissue **cancer** , somatostatin-secreting tumor, spine **cancer** , squamous cell carcinoma, stomach **cancer** , striated muscle **cancer** , submesothelial **cancer** , superficial spreading melanoma, T cell leukemia, testicular **cancer** , thyroid **cancer** , tongue **cancer** , undifferentiated carcinoma, ureter **cancer** , urethra **cancer** , urinary bladder **cancer** , urinary system **cancer** , **uterine cervix - cancer** , **uterine** corpus **cancer** , uveal melanoma, vaginal **cancer** , verrucous carcinoma, VIPoma, vulva **cancer** , well differentiated carcinoma, and Wilms tumor...

...lymphocytic leukemia, acute myeloid leukemia, adenocarcinoma, adenoid cycstic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, anal canal **cancer** , anal **cancer** , anorectum **cancer** , astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, biliary **cancer** , bone **cancer** , bone marrow **cancer** , brain **cancer** , breast **cancer** , bronchial **cancer** , bronchial gland carcinomas, carcinoids, carcinoma, **carcinosarcoma** , cholangiocarcinoma, chondosarcoma, choriod plexus papilloma/carcinoma, chronic lymphocytic leukemia, chronic myeloid leukemia, clear cell carcinoma, colon **cancer** , colorectal **cancer** , connective tissue **cancer** , cystadenoma, digestive system **cancer** , duodenum **cancer** , endocrine system **cancer** , endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, endothelial cell **cancer** , ependymal **cancer** , epithelial cell **cancer** , esophageal **cancer** , Ewing's sarcoma, eye and orbit **cancer** , female genital **cancer** , focal nodular hyperplasia, gallbladder **cancer** , gastric antrum **cancer** , gastric fundus **cancer** , gastrinoma, germ cell tumors, glioblastoma, glucagonoma, heart **cancer** , hemangiblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatobiliary **cancer** , hepatocellular carcinoma, Hodgkin's disease, ileum **cancer** , insulinoma, intaepithelial neoplasia, interepithelial squamous cell neoplasia, intrahepatic bile duct **cancer** , invasive squamous cell carcinoma, jejunum **cancer** , joint **cancer** , Kaposi's sarcoma, kidney and renal pelvic **cancer** , large cell carcinoma, large intestine **cancer** , larynx **cancer** , leiomyosarcoma, lentigo maligna melanomas, leukemia, liver **cancer** , lung **cancer** , lymphoma, male genital **cancer** , malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal **cancer** , mesothelial **cancer** , metastatic carcinoma, mouth

cancer , mucoepidermoid carcinoma, multiple myeloma, muscle **cancer** , nasal tract **cancer** , nervous system **cancer** , neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, non-epithelial skin **cancer** , non-Hodgkin's lymphoma, oat cell carcinoma, oligodendroglial **cancer** , oral cavity **cancer** , osteosarcoma, ovarian **cancer** , pancreatic **cancer** , papillary serous adenocarcinoma, penile **cancer** , pharynx **cancer** , pituitary tumors, plasmacytoma, prostate **cancer** , pseudosarcoma, pulmonary blastoma, rectal **cancer** , renal cell carcinoma, respiratory system **cancer** , retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, sinus **cancer** , skin **cancer** , small cell carcinoma, small intestine **cancer** , smooth muscle **cancer** , soft tissue **cancer** , somatostatin-secreting tumor, spine **cancer** , squamous cell carcinoma, stomach **cancer** , striated muscle **cancer** , submesothelial **cancer** , superficial spreading melanoma, T cell leukemia, testicular **cancer** , thyroid **cancer** , tongue **cancer** , undifferentiated carcinoma, ureter **cancer** , urethra **cancer** , urinary bladder **cancer** , urinary system **cancer** , **uterine cervix cancer** , **uterine** corpus **cancer** , uveal melanoma, vaginal **cancer** , verrucous carcinoma, VIPoma, vulva **cancer** , well differentiated carcinoma, and Wilms tumor. 16 The method of claim 14 wherein the neoplasia...

...disorders, bacterial-induced inflammation, Behcet's syndrome, bone resorption, brain edema, bronchitis, burns, bursitis, cachexia, **cancer** pain, central nervous system disorders, cerebral amyloid angiopathy, cerebral ischemia, Chlamydia-induced inflammation, chronic obstructive ...disorders, bacterial-induced inflammation, Behcet's syndrome, bone resorption, brain edema, bronchitis, burns, bursitis, cachexia, **cancer** pain, central nervous system disorders, cerebral amyloid angiopathy, cerebral ischemia, Chlamydia-induced inflammation, chronic obstructive ...

10/3,K,AB/2

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METHOD OF USING A COX-2 INHIBITOR AND AN ALKYLATING-TYPE ANTINEOPLASTIC AGENT AS A COMBINATION THERAPY IN THE TREATMENT OF NEOPLASIA

Inventors: Masferrer Jaime L (US)
Assignee: Pharmacia Corp
Assignee Code: 63809

Publication (No,Kind,Date), Applic (No,Date):
US 20040072889 A1 20040415 US 2003414867 20030416
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Provisional Applic(No,Date): US 60-44485 19970421; US 60-113786 19981223

Abstract: The present invention provides compositions and methods to treat, prevent or inhibit a neoplasia or a neoplasia-related disorder in a mammal using a combination of a COX-2 inhibitor and an alkylating-type antineoplastic agent.

Non-exemplary Claims: ...lymphocytic leukemia, acute myeloid leukemia, adenocarcinoma, adenoid cycstic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, anal canal **cancer** , anal **cancer** , anorectum **cancer** , astrocytic tumors, bartholin gland carcinoma, basal cell

carcinoma, biliary **cancer** , bone **cancer** , bone marrow **cancer** , brain **cancer** , breast **cancer** , bronchial **cancer** , bronchial gland carcinomas, carcinoids, carcinoma, **carcinosarcoma** , cholangiocarcinoma, chondosarcoma, choriod plexus papilloma/carcinoma, chronic lymphocytic leukemia, chronic myeloid leukemia, clear cell carcinoma, colon **cancer** , colorectal **cancer** , connective tissue **cancer** , cystadenoma, digestive system **cancer** , duodenum **cancer** , endocrine system **cancer** , endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, endothelial cell **cancer** , ependymal **cancer** , epithelial cell **cancer** , esophageal **cancer** , Ewing's sarcoma, eye and orbit **cancer** , female genital **cancer** , focal nodular hyperplasia, gallbladder **cancer** , gastric antrum **cancer** , gastric fundus **cancer** , gastrinoma, germ cell tumors, glioblastoma, glucagonoma, heart **cancer** , hemangiblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatobiliary **cancer** , hepatocellular carcinoma, Hodgkin's disease, ileum **cancer** , insulinoma, intaepithelial neoplasia, interepithelial squamous cell neoplasia, intrahepatic bile duct **cancer** , invasive squamous cell carcinoma, jejunum **cancer** , joint **cancer** , Kaposi's sarcoma, kidney and renal pelvic **cancer** , large cell carcinoma, large intestine **cancer** , larynx **cancer** , leiomyosarcoma, lentigo maligna melanomas, leukemia, liver **cancer** , lung **cancer** , lymphoma, male genital **cancer** , malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal **cancer** , mesothelial **cancer** , metastatic carcinoma, mouth **cancer** , mucoepidermoid carcinoma, multiple myeloma, muscle **cancer** , nasal tract **cancer** , nervous system **cancer** , neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, non-epithelial skin **cancer** , non-Hodgkin's lymphoma, oat cell carcinoma, oligodendroglial **cancer** , oral cavity **cancer** , osteosarcoma, ovarian **cancer** , pancreatic **cancer** , papillary serous adenocarcinoma, penile **cancer** , pharynx **cancer** , pituitary tumors, plasmacytoma, prostate **cancer** , pseudosarcoma, pulmonary blastoma, rectal **cancer** , renal cell carcinoma, respiratory system **cancer** , retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, sinus **cancer** , skin **cancer** , small cell carcinoma, small intestine **cancer** , smooth muscle **cancer** , soft tissue **cancer** , somatostatin-secreting tumor, spine **cancer** , squamous cell carcinoma, stomach **cancer** , striated muscle **cancer** , submesothelial **cancer** , superficial spreading melanoma, T cell leukemia, testicular **cancer** , thyroid **cancer** , tongue **cancer** , undifferentiated carcinoma, ureter **cancer** , urethra **cancer** , urinary bladder **cancer** , urinary system **cancer** , **uterine cervix cancer** , **uterine** corpus **cancer** , uveal melanoma, vaginal **cancer** , verrucous carcinoma, VIPoma, vulva **cancer** , well differentiated carcinoma, and Wilms tumor...

...lymphocytic leukemia, acute myeloid leukemia, adenocarcinoma, adenoid cycstic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, anal canal **cancer** , anal **cancer** , anorectum **cancer** , astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, biliary **cancer** , bone **cancer** , bone marrow **cancer** , brain **cancer** , breast **cancer** , bronchial **cancer** , bronchial gland carcinomas, carcinoids, carcinoma, **carcinosarcoma** , cholangiocarcinoma, chondosarcoma, choriod plexus papilloma/carcinoma, chronic lymphocytic leukemia, chronic myeloid leukemia, clear cell carcinoma, colon **cancer** , colorectal **cancer** , connective tissue **cancer** , cystadenoma, digestive system **cancer** , duodenum **cancer** , endocrine system **cancer** , endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, endothelial cell **cancer** , ependymal **cancer** , epithelial cell **cancer** , esophageal **cancer** , Ewing's sarcoma, eye and

orbit **cancer** , female genital **cancer** , focal nodular hyperplasia, gallbladder **cancer** , gastric antrum **cancer** , gastric fundus **cancer** , gastrinoma, germ cell tumors, glioblastoma, glucagonoma, heart **cancer** , hemangiblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatobiliary **cancer** , hepatocellular carcinoma, Hodgkin's disease, ileum **cancer** , insulinoma, intaepithelial neoplasia, interepithelial squamous cell neoplasia, intrahepatic bile duct **cancer** , invasive squamous cell carcinoma, jejunum **cancer** , joint **cancer** , Kaposi's sarcoma, kidney and renal pelvic **cancer** , large cell carcinoma, large intestine **cancer** , larynx **cancer** , leiomyosarcoma, lentigo maligna melanomas, leukemia, liver **cancer** , lung **cancer** , lymphoma, male genital **cancer** , malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal **cancer** , mesothelial **cancer** , metastatic carcinoma, mouth **cancer** , mucoepidermoid carcinoma, multiple myeloma, muscle **cancer** , nasal tract **cancer** , nervous system **cancer** , neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, non-epithelial skin **cancer** , non-Hodgkin's lymphoma, oat cell carcinoma, oligodendroglial **cancer** , oral cavity **cancer** , osteosarcoma, ovarian **cancer** , pancreatic **cancer** , papillary serous adenocarcinoma, penile **cancer** , pharynx **cancer** , pituitary tumors, plasmacytoma, prostate **cancer** , pseudosarcoma, pulmonary blastoma, rectal **cancer** , renal cell carcinoma, respiratory system **cancer** , retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, sinus **cancer** , skin **cancer** , small cell carcinoma, small intestine **cancer** , smooth muscle **cancer** , soft tissue **cancer** , somatostatin-secreting tumor, spine **cancer** , squamous cell carcinoma, stomach **cancer** , striated muscle **cancer** , submesothelial **cancer** , superficial spreading melanoma, T cell leukemia, testicular **cancer** , thyroid **cancer** , tongue **cancer** , undifferentiated carcinoma, ureter **cancer** , urethra **cancer** , urinary bladder **cancer** , urinary system **cancer** , **uterine cervix cancer** , **uterine** corpus **cancer** , uveal melanoma, vaginal **cancer** , verrucous carcinoma, VIPoma, vulva **cancer** , well differentiated carcinoma, and Wilms tumor...

10/3,K,AB/3

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Document Type: C

METHOD OF USING A COX-2 INHIBITOR AND AN AROMATASE INHIBITOR AS A COMBINATION THERAPY

Inventors: Masferrer Jaime L (US)
Assignee: Pharmacia Corp
Assignee Code: 63809

Publication (No,Kind,Date), Applic (No,Date):
US 20040053900 A1 20040318 US 2003421685 20030423
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Provisional Applic(No,Date): US 60-113786 19981223

Abstract: The present invention provides compositions and methods to treat, prevent or inhibit a neoplasia, a neoplasia-related disorder or osteoporosis in a mammal using a combination of a COX-2 inhibitor and an aromatase inhibitor.

Non-exemplary Claims: ...lymphocytic leukemia, acute myeloid leukemia, adenocarcinoma, adenoid cycstic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, anal canal **cancer** , anal **cancer** , anorectum **cancer** , astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, biliary **cancer** , bone **cancer** , bone marrow **cancer** , brain **cancer** , breast **cancer** , bronchial **cancer** , bronchial gland carcinomas, carcinoids, carcinoma, **carcinosarcoma** , cholangiocarcinoma, chondosarcoma, choriod plexus papilloma/carcinoma, chronic lymphocytic leukemia, chronic myeloid leukemia, clear cell carcinoma, colon **cancer** , colorectal **cancer** , connective tissue **cancer** , cystadenoma, digestive system **cancer** , duodenum **cancer** , endocrine system **cancer** , endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, endothelial cell **cancer** , ependymal **cancer** , epithelial cell **cancer** , esophageal **cancer** , Ewing's sarcoma, eye and orbit **cancer** , female genital **cancer** , focal nodular hyperplasia, gallbladder **cancer** , gastric antrum **cancer** , gastric fundus **cancer** , gastrinoma, germ cell tumors, glioblastoma, glucagonoma, heart **cancer** , hemangiblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatobiliary **cancer** , hepatocellular carcinoma, Hodgkin's disease, ileum **cancer** , insulinoma, intaepithelial neoplasia, interepithelial squamous cell neoplasia, intrahepatic bile duct **cancer** , invasive squamous cell carcinoma, jejunum **cancer** , joint **cancer** , Kaposi's sarcoma, kidney and renal pelvic **cancer** , large cell carcinoma, large intestine **cancer** , larynx **cancer** , leiomyosarcoma, lentigo maligna melanomas, leukemia, liver **cancer** , lung **cancer** , lymphoma, male genital **cancer** , malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal **cancer** , mesothelial **cancer** , metastatic carcinoma, mouth **cancer** , mucoepidermoid carcinoma, multiple myeloma, muscle **cancer** , nasal tract **cancer** , nervous system **cancer** , neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, non-epithelial skin **cancer** , non-Hodgkin's lymphoma, oat cell carcinoma, oligodendroglial **cancer** , oral cavity **cancer** , osteosarcoma, ovarian **cancer** , pancreatic **cancer** , papillary serous adenocarcinoma, penile **cancer** , pharynx **cancer** , pituitary tumors, plasmacytoma, prostate **cancer** , pseudosarcoma, pulmonary blastoma, rectal **cancer** , renal cell carcinoma, respiratory system **cancer** , retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, sinus **cancer** , skin **cancer** , small cell carcinoma, small intestine **cancer** , smooth muscle **cancer** , soft tissue **cancer** , somatostatin-secreting tumor, spine **cancer** , squamous cell carcinoma, stomach **cancer** , striated muscle **cancer** , submesothelial **cancer** , superficial spreading melanoma, T cell leukemia, testicular **cancer** , thyroid **cancer** , tongue **cancer** , undifferentiated carcinoma, ureter **cancer** , urethra **cancer** , urinary bladder **cancer** , urinary system **cancer** , **uterine cervix cancer** , **uterine** corpus **cancer** , uveal melanoma, vaginal **cancer** , verrucous carcinoma, VIPoma, vulva **cancer** , well differentiated carcinoma, and Wilms tumor...

...lymphocytic leukemia, acute myeloid leukemia, adenocarcinoma, adenoid cycstic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, anal canal **cancer** , anal **cancer** , anorectum **cancer** , astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, biliary **cancer** , bone **cancer** , bone marrow **cancer** , brain **cancer** , breast **cancer** , bronchial **cancer** , bronchial gland carcinomas, carcinoids, carcinoma, **carcinosarcoma** , cholangiocarcinoma, chondosarcoma, choriod plexus papilloma/carcinoma, chronic lymphocytic leukemia, chronic myeloid leukemia, clear cell carcinoma, colon **cancer** , colorectal **cancer** ,

connective tissue **cancer** , cystadenoma, digestive system **cancer** , duodenum **cancer** , endocrine system **cancer** , endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, endothelial cell **cancer** , ependymal **cancer** , epithelial cell **cancer** , esophageal **cancer** , Ewing's sarcoma, eye and orbit **cancer** , female genital **cancer** , focal nodular hyperplasia, gallbladder **cancer** , gastric antrum **cancer** , gastric fundus **cancer** , gastrinoma, germ cell tumors, glioblastoma, glucagonoma, heart **cancer** , hemangiblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatobiliary **cancer** , hepatocellular carcinoma, Hodgkin's disease, ileum **cancer** , insulinoma, intaepithelial neoplasia, interepithelial squamous cell neoplasia, intrahepatic bile duct **cancer** , invasive squamous cell carcinoma, jejunum **cancer** , joint **cancer** , Kaposi's sarcoma, kidney and renal pelvic **cancer** , large cell carcinoma, large intestine **cancer** , larynx **cancer** , leiomyosarcoma, lentigo maligna melanomas, leukemia, liver **cancer** , lung **cancer** , lymphoma, male genital **cancer** , malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal **cancer** , mesothelial **cancer** , metastatic carcinoma, mouth **cancer** , mucoepidermoid carcinoma, multiple myeloma, muscle **cancer** , nasal tract **cancer** , nervous system **cancer** , neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, non-epithelial skin **cancer** , non-Hodgkin's lymphoma, oat cell carcinoma, oligodendroglial **cancer** , oral cavity **cancer** , osteosarcoma, ovarian **cancer** , pancreatic **cancer** , papillary serous adenocarcinoma, penile **cancer** , pharynx **cancer** , pituitary tumors, plasmacytoma, prostate **cancer** , pseudosarcoma, pulmonary blastoma, rectal **cancer** , renal cell carcinoma, respiratory system **cancer** , retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, sinus **cancer** , skin **cancer** , small cell carcinoma, small intestine **cancer** , smooth muscle **cancer** , soft tissue **cancer** , somatostatin-secreting tumor, spine **cancer** , squamous cell carcinoma, stomach **cancer** , striated muscle **cancer** , submesothelial **cancer** , superficial spreading melanoma, T cell leukemia, testicular **cancer** , thyroid **cancer** , tongue **cancer** , undifferentiated carcinoma, ureter **cancer** , urethra **cancer** , urinary bladder **cancer** , urinary system **cancer** , **uterine cervix cancer** , **uterine** corpus **cancer** , uveal melanoma, vaginal **cancer** , verrucous carcinoma, VIPoma, vulva **cancer** , well differentiated carcinoma, and Wilms tumor...

10/3,K,AB/4

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IFI Publication Control No: 2003-0225150 IFI Chemical Acc No: 2003-0068096
Document Type: C

METHOD OF USING A COX-2 INHIBITOR AND A TOPOISOMERASE II INHIBITOR AS A COMBINATION THERAPY IN THE TREATMENT OF NEOPLASIA; PROVIDED THAT THE COX-2 INHIBITOR COMPOUND SOURCE IS NOT A 2,3-SUBSTITUTED INDOLE COMPOUND OR A TETRACYCLIC SULFONYLBENZENE COMPOUND; CELECOXIB AND ACLARUBICIN FOR EXAMPLE

Inventors: Masferrer Jaime L (US)
Assignee: Pharmacia Corp
Assignee Code: 63809

Publication (No,Kind,Date), Applic (No,Date):
US 20030225150 A1 20031204 US 2002323065 20021218
Priority Applic(No,Date): US 2002323065 20021218; US 98175584 19981020; US 2000569383 20000511; US 9862537 19980417; US 99470951

19991222; US 2001865177 20010524
Provisional Applic(No,Date): US 60-44485 19970421; US 60-113786 19981223

Abstract: The present invention provides compositions and methods to treat, prevent or inhibit a neoplasia or a neoplasia-related disorder in a mammal using a combination of a COX-2 inhibitor and a topoisomerase II inhibitor.

Non-exemplary Claims: ...lymphocytic leukemia, acute myeloid leukemia, adenocarcinoma, adenoid cycstic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, anal canal **cancer** , anal **cancer** , anorectum **cancer** , astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, biliary **cancer** , bone **cancer** , bone marrow **cancer** , brain **cancer** , breast **cancer** , bronchial **cancer** , bronchial gland carcinomas, carcinoids, carcinoma, **carcinosarcoma** , cholangiocarcinoma, chondosarcoma, choriod plexus papilloma/carcinoma, chronic lymphocytic leukemia, chronic myeloid leukemia, clear cell carcinoma, colon **cancer** , colorectal **cancer** , connective tissue **cancer** , cystadenoma, digestive system **cancer** , duodenum **cancer** , endocrine system **cancer** , endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, endothelial cell **cancer** , ependymal **cancer** , epithelial cell **cancer** , esophageal **cancer** , Ewing's sarcoma, eye and orbit **cancer** , female genital **cancer** , focal nodular hyperplasia, gallbladder **cancer** , gastric antrum **cancer** , gastric fundus **cancer** , gastrinoma, germ cell tumors, glioblastoma, glucagonoma, heart **cancer** , hemangiblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatobiliary **cancer** , hepatocellular carcinoma, Hodgkin's disease, ileum **cancer** , insulinoma, intaepithelial neoplasia, interepithelial squamous cell neoplasia, intrahepatic bile duct **cancer** , invasive squamous cell carcinoma, jejunum **cancer** , joint **cancer** , Kaposi's sarcoma, kidney and renal pelvic **cancer** , large cell carcinoma, large intestine **cancer** , larynx **cancer** , leiomyosarcoma, lentigo maligna melanomas, leukemia, liver **cancer** , lung **cancer** , lymphoma, male genital **cancer** , malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal **cancer** , mesothelial **cancer** , metastatic carcinoma, mouth **cancer** , mucoepidermoid carcinoma, multiple myeloma, muscle **cancer** , nasal tract **cancer** , nervous system **cancer** , neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, non-epithelial skin **cancer** , non-Hodgkin's lymphoma, oat cell carcinoma, oligodendroglial **cancer** , oral cavity **cancer** , osteosarcoma, ovarian **cancer** , pancreatic **cancer** , papillary serous adenocarcinoma, penile **cancer** , pharynx **cancer** , pituitary tumors, plasmacytoma, prostate **cancer** , pseudosarcoma, pulmonary blastoma, rectal **cancer** , renal cell carcinoma, respiratory system **cancer** , retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, sinus **cancer** , skin **cancer** , small cell carcinoma, small intestine **cancer** , smooth muscle **cancer** , soft tissue **cancer** , somatostatin-secreting tumor, spine **cancer** , squamous cell carcinoma, stomach **cancer** , striated muscle **cancer** , submesothelial **cancer** , superficial spreading melanoma, T cell leukemia, testicular **cancer** , thyroid **cancer** , tongue **cancer** , undifferentiated carcinoma, ureter **cancer** , urethra **cancer** , urinary bladder **cancer** , urinary system **cancer** , **uterine cervix cancer** , **uterine** corpus **cancer** , uveal melanoma, vaginal **cancer** , verrucous carcinoma, VIPoma, vulva **cancer** , well differentiated carcinoma, and Wilms tumor...

...The composition of claim 17 wherein the neoplasia or the

neoplasia-related disorder is breast **cancer** .

...

...composition of claim 17 wherein the neoplasia or the neoplasia-related disorder is urinary bladder **cancer** .

...

...lymphocytic leukemia, acute myeloid leukemia, adenocarcinoma, adenoid cycstic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, anal canal **cancer** , anal **cancer** , anorectum **cancer** , astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, biliary **cancer** , bone **cancer** , bone marrow **cancer** , brain **cancer** , breast **cancer** , bronchial **cancer** , bronchial gland carcinomas, carcinoids, carcinoma, **carcinosarcoma** , cholangiocarcinoma, chondosarcoma, choriod plexus papilloma/carcinoma, chronic lymphocytic leukemia, chronic myeloid leukemia, clear cell carcinoma, colon **cancer** , colorectal **cancer** , connective tissue **cancer** , cystadenoma, digestive system **cancer** , duodenum **cancer** , endocrine system **cancer** , endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, endothelial cell **cancer** , ependymal **cancer** , epithelial cell **cancer** , esophageal **cancer** , Ewing's sarcoma, eye and orbit **cancer** , female genital **cancer** , focal nodular hyperplasia, gallbladder **cancer** , gastric antrum **cancer** , gastric fundus **cancer** , gastrinoma, germ cell tumors, glioblastoma, glucagonoma, heart **cancer** , hemangiblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatobiliary **cancer** , hepatocellular carcinoma, Hodgkin's disease, ileum **cancer** , insulinoma, intaepithelial neoplasia, interepithelial squamous cell neoplasia, intrahepatic bile duct **cancer** , invasive squamous cell carcinoma, jejunum **cancer** , joint **cancer** , Kaposi's sarcoma, kidney and renal pelvic **cancer** , large cell carcinoma, large intestine **cancer** , larynx **cancer** , leiomyosarcoma, lentigo maligna melanomas, leukemia, liver **cancer** , lung **cancer** , lymphoma, male genital **cancer** , malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal **cancer** , mesothelial **cancer** , metastatic carcinoma, mouth **cancer** , mucoepidermoid carcinoma, multiple myeloma, muscle **cancer** , nasal tract **cancer** , nervous system **cancer** , neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, non-epithelial skin **cancer** , non-Hodgkin's lymphoma, oat cell carcinoma, oligodendroglial **cancer** , oral cavity **cancer** , osteosarcoma, ovarian **cancer** , pancreatic **cancer** , papillary serous adenocarcinoma, penile **cancer** , pharynx **cancer** , pituitary tumors, plasmacytoma, prostate **cancer** , pseudosarcoma, pulmonary blastoma, rectal **cancer** , renal cell carcinoma, respiratory system **cancer** , retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, sinus **cancer** , skin **cancer** , small cell carcinoma, small intestine **cancer** , smooth muscle **cancer** , soft tissue **cancer** , somatostatin-secreting tumor, spine **cancer** , squamous cell carcinoma, stomach **cancer** , striated muscle **cancer** , submesothelial **cancer** , superficial spreading melanoma, T cell leukemia, testicular **cancer** , thyroid **cancer** , tongue **cancer** , undifferentiated carcinoma, ureter **cancer** , urethra **cancer** , urinary bladder **cancer** , urinary system **cancer** , **uterine cervix cancer** , **uterine** corpus **cancer** , uveal melanoma, vaginal **cancer** , verrucous carcinoma, VIPoma, vulva **cancer** , well differentiated carcinoma, and Wilms tumor...

...The method of claim 39 wherein the neoplasia or the neoplasia-related disorder is breast **cancer** .

...

...method of claim 39 wherein the neoplasia or the neoplasia-related disorder is urinary bladder **cancer** .

10/3,K,AB/5
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10324212 IFI Acc No: 2003-0068626
IFI Publication Control No: 2003-0068626 IFI Chemical Acc No: 2003-0018528
Document Type: C
PIN1 AS A MARKER FOR ABNORMAL CELL GROWTH; DETECTION OF ABERRANT CELL PROPAGATION IN MAMMALS; OBTAIN CELL SAMPLE, MONITOR EXPRESION OF MARKER GENE, AMPLIFIED EXPRESSION INDICATE ABERRANT CELL PROPAGATION
Inventors: Bao Lere (US); Wang Da Gong (US)
Publication (No,Kind,Date), Applic (No,Date):
US 20030068626 A1 20030410 US 200271747 20020208
Priority Applic(No,Date): US 200271747 20020208
Provisional Applic(No,Date): US 60-267575 20010209

Abstract: Methods for the use of Pin1 as a marker of abnormal cell growth are disclosed. In one embodiment, the method includes detecting a level of Pin1 to stage an abnormal cell growth, such as breast or prostate **cancer** . In another embodiment, the method includes evaluating the efficacy of a treatment of an abnormal cell growth, such as **cancer** , by monitoring the levels of Pin1. In another embodiment, the method includes evaluating the extent of metastasis of abnormal cell growth, such as **cancer** . The levels of Pin1 can be protein levels or nucleic acid levels.
Abstract: ...a level of Pin1 to stage an abnormal cell growth, such as breast or prostate **cancer** . In another embodiment, the method includes evaluating the efficacy of a treatment of an abnormal cell growth, such as **cancer** , by monitoring the levels of Pin1. In another embodiment, the method includes evaluating the extent of metastasis of abnormal cell growth, such as **cancer** . The levels of Pin1 can be protein levels or nucleic acid levels.
Non-exemplary Claims: ...the group consisting of rectum, the brain, the mouth, central nervous system, breast tissue, the **uterine cervix** , the endometrium, the head/neck, the skin, parotid tissue, the prostate, the brain, the gall...

...8. The method of claim 1, wherein the abnormal cell growth is **cancer** .
...

...9. The method of claim 8, wherein the **cancer** is selected from the group consisting of oligodendroglioma, astrocytoma, glioblastomamultiforme, cervical carcinoma, endometriod carcinoma, endometrium serous carcenoma, ovary endometroid **cancer** , ovary Brenner tumor, ovary mucinous **cancer** , ovary serous **cancer** , uterus **carcinosarcoma** , breast lobular **cancer** , breast ductal **cancer** , breast medullary **cancer** , breast mucinous **cancer** , breast tubular **cancer** , thyroid adenocarcinoma, thyroid follicular **cancer** , thyroid medullary **cancer** , thyroid papillary carcinoma, parathyroid adenocarcinoma, adrenal gland adenoma, adrenal gland **cancer** , pheochromocytoma, colon adenoma mild displasia, colon adenoma moderate displasia, colon adenoma severe displasia, colon adenocarcinoma, esophagus adenocarcinoma, hepatocelluar carcinoma, mouth **cancer** , gall bladder adenocarcinoma, pancreatic adenocarcinoma, small intestine adenocarcinoma, stomach diffuse adenocarcinoma, prostate (hormone-refract), prostate...

...kideny chromophobic carcinoma, kidney clear cell carcinoma, kidney oncocytoma, kideny papillary carcinoma, testis non-seminomatous **cancer** , testis seminoma, urinary bladder transitional carcinoma, lung adenocarcinoma, lung large cell **cancer** , lung small cell **cancer** , lung squmous cell carcinoma, Hodgkin lymphoma, MALT lymphoma, non-hodgkins lymphoma (NHL) diffuse large B, NHL, thymoma, skin malignant melanoma, skin basolioma, skin squamous cell **cancer** , skin merkel zell **cancer** , skin benign nevus, lipoma, and liposarcoma...18. A method of determining the stage of **cancer** in a test sample from a mammal, comprising assessing a level of Pin1 in the test sample, wherein the level of Pin1 correlates with the stage of the **cancer** .

...28. The method of claim 18, wherein the **cancer** is selected from the group consisting of oligodendroglioma, astrocytoma, glioblastomamultiforme, cervical carcinoma, endometriod carcinoma, endometrium serous carcenoma, ovary endometroid **cancer** , ovary Brenner tumor, ovary mucinous **cancer** , ovary serous **cancer** , uterus **carcinosarcoma** , breast lobular **cancer** , breast ductal **cancer** , breast medullary **cancer** , breast mucinous **cancer** , breast tubular **cancer** , thyroid adenocarcinoma, thyroid follicular **cancer** , thyroid medullary **cancer** , thyroid papillary carcinoma, parathyroid adenocarcinoma, adrenal gland adenoma, adrenal gland **cancer** , pheochromocytoma, colon adenoma mild displasia, colon adenoma moderate displasia, colon adenoma severe displasia, colon adenocarcinoma, esophagus adenocarcinoma, hepatocelluar carcinoma, mouth **cancer** , gall bladder adenocarcinoma, pancreatic adenocarcinoma, small intestine adenocarcinoma, stomach diffuse adenocarcinoma, prostate (hormone-refract), prostate...

...kideny chromophobic carcinoma, kidney clear cell carcinoma, kidney oncocytoma, kideny papillary carcinoma, testis non-seminomatous **cancer** , testis seminoma, urinary bladder transitional carcinoma, lung adenocarcinoma, lung large cell **cancer** , lung small cell **cancer** , lung squmous cell carcinoma, Hodgkin lymphoma, MALT lymphoma, non-hodgkins lymphoma (NHL) diffuse large B, NHL, thymoma, skin malignant melanoma, skin basolioma, skin squamous cell **cancer** , skin merkel zell **cancer** , skin benign nevus, lipoma, and liposarcoma...

...29. A method of claim 18 wherein the stage of **cancer** is determined by assessing a level of a Pin1 nucleic acid in a test sample...

...30. A method of claim 18 wherein the stage of **cancer** is determined by assessing a level of a Pin1 nucleic acid in a test sample...45. A method for determining whether a subject having **cancer** is likely to respond to treatment comprising a Pin1 inhibitor compound, the method comprising: assessing...

...46. The method of claim 45 wherein the **cancer** is selected from the group consisting of oligodendroglioma, astrocytoma, glioblastomamultiforme, cervical carcinoma, endometriod carcinoma, endometrium serous carcenoma, ovary endometroid **cancer** , ovary Brenner tumor, ovary mucinous **cancer** , ovary serous **cancer** , uterus **carcinosarcoma** , breast lobular **cancer** , breast ductal **cancer** , breast medullary **cancer** , breast mucinous **cancer** , breast tubular **cancer** , thyroid adenocarcinoma, thyroid follicular **cancer** , thyroid medullary **cancer** , thyroid papillary carcinoma, parathyroid adenocarcinoma, adrenal gland adenoma, adrenal gland **cancer** , pheochromocytoma, colon adenoma mild displasia, colon adenoma moderate displasia, colon adenoma severe displasia, colon adenocarcinoma, esophagus adenocarcinoma, hepatocelluar carcinoma, mouth **cancer** , gall bladder adenocarcinoma, pancreatic adenocarcinoma, small intestine adenocarcinoma, stomach diffuse adenocarcinoma, prostate (hormone-refract), prostate...

...kideny chromophobic carcinoma, kidney clear cell carcinoma, kidney oncocytoma, kideny papillary carcinoma, testis non-seminomatous **cancer** , testis seminoma, urinary bladder transitional carcinoma, lung adenocarcinoma, lung large cell **cancer** , lung small cell **cancer** , lung squmous cell carcinoma, Hodgkin lymphoma, MALT lymphoma, non-hodgkins lymphoma (NHL) diffuse large B, NHL, thymoma, skin malignant melanoma, skin basolioma, skin squamous cell **cancer** , skin merkel zell **cancer** , skin benign nevus, lipoma, and liposarcoma...

...47. A method of treating an individual suffering from **cancer** comprising, administering to said individaul a Pin1 inhibitor such that treatment occurs...

...48. The method of claim 47 wherein said **cancer** is selected from the group consisting of oligodendroglioma, astrocytoma, glioblastomamultiforme, cervical carcinoma, endometriod carcinoma, endometrium serous carcenoma, ovary endometroid **cancer** , ovary Brenner tumor, ovary mucinous **cancer** , ovary serous **cancer** , uterus **carcinosarcoma** , breast lobular **cancer** , breast ductal **cancer** , breast medullary **cancer** , breast mucinous **cancer** , breast tubular **cancer** , thyroid adenocarcinoma, thyroid follicular **cancer** , thyroid medullary **cancer** , thyroid papillary carcinoma, parathyroid adenocarcinoma, adrenal gland adenoma, adrenal gland **cancer** , pheochromocytoma, colon adenoma mild displasia, colon adenoma moderate displasia, colon adenoma severe displasia, colon adenocarcinoma, esophagus adenocarcinoma, hepatocelluar carcinoma, mouth **cancer** , gall bladder adenocarcinoma, pancreatic adenocarcinoma, small intestine adenocarcinoma, stomach diffuse adenocarcinoma, prostate (hormone-refract), prostate...

...kideny chromophobic carcinoma, kidney clear cell carcinoma, kidney oncocytoma, kideny papillary carcinoma, testis non-seminomatous **cancer** , testis seminoma, urinary bladder transitional carcinoma, lung adenocarcinoma, lung large cell **cancer** , lung small cell **cancer** , lung squmous cell carcinoma, Hodgkin lymphoma, MALT lymphoma, non-hodgkins lymphoma (NHL) diffuse large B, NHL, thymoma, skin malignant melanoma, skin basolioma, skin squamous cell **cancer** , skin merkel zell **cancer** , skin benign nevus, lipoma, and liposarcoma.
?

Uterine adenosarcoma: a clinicopathologic study of 11 cases with a reevaluation of histologic criteria.

Czernobilsky B; Hohlweg-Majert P; Dallenbach-Hellweg G

Archives of gynecology (GERMANY, WEST) **1983** , 233 (4) p281-94, ISSN 0170-9925 Journal Code: 7901051

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Eleven biphasic uterine tumors with epithelial components and homologous stroma were reevaluated. Originally these were diagnosed as adenofibroma, adenosarcoma, carcinosarcoma, or mixtures thereof, but were now reclassified as adenosarcomas of which seven were "pure" and four mixed with foci of carcinosarcoma. Nine of the tumors arose in the endometrium and two in the endocervix. The mean patient's age was 55 years. The most common complaint was vaginal bleeding. Macroscopically these tumors presented as polypoid masses. The epithelial componen

Sarcomas and carcinosarcomas of the uterine cervix .
Abell M R; Ramirez J A
Cancer (UNITED STATES) May **1973** , 31 (5) p1176-92, ISSN 0008-543X
Journal Code: 0374236
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Sarcomas and carcinosarcomas of the uterine cervix .

1117728 Genuine Article#: FX732 Number of References: 23

Title: REQUIREMENT OF THE AUXIN POLAR TRANSPORT-SYSTEM IN EARLY STAGES OF ARABIDOPSIS FLORAL BUD FORMATION (Abstract Available)

Author(s): OKADA K; UEDA J; KOMAKI MK; BELL CJ; SHIMURA Y
Corporate Source: NATL INST BASIC BIOL,DIV GENE EXPRESS & REGULAT1/OKAZAKI/AICHI 444/JAPAN/; UNIV OSAKA PREFECTURE,COLL INTEGRATED ARTS & SCI/SAKAI/OSAKA 591/JAPAN/; KYOTO UNIV,FAC SCI,DEPT BIOPHYS/KYOTO 606//JAPAN/

Journal: PLANT CELL, 1991, V3, N7, P677-684
Language: ENGLISH Document Type: ARTICLE

Abstract: The pin-formed mutant **pin 1** -1, one of the Arabidopsis flower mutants, has several structural abnormalities in inflorescence axes, flowers, and leaves. In some cases, **pin 1** -1 forms a flower with abnormal structure (wide petals, no stamens, pistil-like structure with no ovules in the **ovary**) at the top of inflorescence axes. In other cases, no floral buds are formed on the axes. An independently isolated allelic mutant (**pin 1** -2) shows similar phenotypes. These mutant phenotypes are exactly the same in wild-type plants cultured in the presence of chemical compounds known as auxin polar transport inhibitors: 9-hydroxyfluorene-9-carboxylic acid or N-(1-naphthyl)phthalamic acid. We tested the polar transport activity of indole-3-acetic acid and the endogenous amount of free indole-3-acetic acid in the tissue of inflorescence axes of the **pin 1** mutants and wild type. The polar transport activity in the **pin 1** -1 mutant and in the **pin 1** -2 mutant was decreased to 14% and 7% of wild type, respectively. These observations strongly suggest that the normal level of polar transport activity in the inflorescence axes is required in early developmental stages of floral bud formation in Arabidopsis and that the primary function of the **pin 1** gene is auxin polar transport in the inflorescence axis.

Abstract: The pin-formed mutant **pin 1** -1, one of the Arabidopsis flower mutants, has several structural abnormalities in inflorescence axes, flowers, and leaves. In some cases, **pin 1** -1 forms a flower with abnormal structure (wide petals, no stamens, pistil-like structure with no ovules in the **ovary**) at the top of inflorescence axes. In other cases, no floral buds are formed on the axes. An independently isolated allelic mutant (**pin 1** -2) shows similar phenotypes. These mutant phenotypes are exactly the same in wild-type plants...

...amount of free indole-3-acetic acid in the tissue of inflorescence axes of the **pin 1** mutants and wild type. The polar transport activity in the **pin 1** -1 mutant and in the **pin 1** -2 mutant was decreased to 14% and 7% of wild type, respectively. These observations strongly...

...developmental stages of floral bud formation in Arabidopsis and that the primary function of the **pin 1** gene is auxin polar transport in the inflorescence axis.

4/3,K,AB/12 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

524721 PMID: 7508950

Human follicular fluid contains pro- and C-terminal immunoreactive alpha-inhibin precursor proteins.

Lambert-Messerlian G M; Isaacson K; Crowley W F; Sluss P; Schneyer A L
Department of Medicine, Massachusetts General Hospital, Boston 02114.

Journal of clinical endocrinology and metabolism (UNITED STATES) Feb 1994, 78 (2) p433-9, ISSN 0021-972X Journal Code: 0375362
Contract/Grant No.: P30-HD-28138; HD; NICHD; T32-HD-07396; HD; NICHD; U54-HD-29164; HD; NICHD; +
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

The majority of immunoactive inhibin in human follicular fluid (hFF) is devoid of pituitary cell bioactivity and is hypothesized to contain alpha-inhibin monomeric proteins known to cross-react with an inhibin antiserum (Monash 1989). The aim of this study was to define more precisely the nature of these inhibin-immunoreactive proteins using alpha-inhibin sequence-specific antisera. First, a polyclonal antiserum was raised to precursor amino acids 21-35 (**PIN - 1**) and was used in a RIA to measure pro-alpha-inhibin-immunoreactive proteins. Western blotting was used to confirm these findings. Secondly, the binding epitope of the Monash antiserum was defined by peptide analysis to be located within the C-terminus (precursor amino acids 326-341) of alpha-inhibin, and this assay was then used to monitor the presence of C-terminal sequences. Similar levels of pro-alpha-inhibin immunoreactivity (**PIN - 1** RIA; N-terminus alpha-inhibin precursor) were detected in hFF collected from women with normal menstrual cycles during the follicular phase and from multiple follicles from a woman undergoing **ovarian** hyperstimulation during an in vitro fertilization (IVF) protocol. Western blotting with the **PIN - 1** antibody confirmed the presence of immunoreactive proteins of 57,000 and 29,000 mol wt in the follicular fluids of both normal cycle and IVF follicles. However, **ovarian** hyperstimulation elevated intrafollicular C-terminal immunoreactivity (Monash RIA) compared to that in normal cycle hFF. Furthermore, intrafollicular estradiol and progesterone were significantly correlated to C-terminal activity in follicles from IVF, but not in normal cycles. These data show that 1) both pro- and C-terminal alpha-inhibin proteins are secreted into follicular fluids from normal and IVF cycles, suggesting that alpha-inhibin precursor proteins may be physiologically relevant in the process of folliculogenesis; and 2) IVF and normal cycle follicular fluids differ in their production and processing of inhibin.

... sequence-specific antisera. First, a polyclonal antiserum was raised to precursor amino acids 21-35 (**PIN - 1**) and was used in a RIA to measure pro-alpha-inhibin-immunoreactive proteins. Western blotting...

... to monitor the presence of C-terminal sequences. Similar levels of pro-alpha-inhibin immunoreactivity (**PIN - 1** RIA; N-terminus alpha-inhibin precursor) were detected in hFF collected from women with normal menstrual cycles during the follicular phase and from multiple follicles from a woman undergoing **ovarian** hyperstimulation during an in vitro fertilization (IVF) protocol. Western blotting with the **PIN - 1** antibody confirmed the presence of immunoreactive proteins of 57,000 and 29,000 mol wt in the follicular fluids of both normal cycle and IVF follicles. However, **ovarian** hyperstimulation elevated intrafollicular C-terminal immunoreactivity (Monash RIA) compared to that in normal cycle hFF...

4/3,K,AB/6 (Item 1 from file: 55)

DIALOG(R)File 55:Biosis Previews(R)

0014794795 BIOSIS NO.: 20040016

4/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

15313453 PMID: 15111319

Prevalent overexpression of prolyl isomerase Pin1 **in human cancers.**

Bao Lere; Kimzey Amy; Sauter Guido; Sowadski Janusz M; Lu Kun Ping; Wang Da-Gong

Pintex Pharmaceuticals Incorporated, Watertown, Massachusetts 02472, USA.

American journal of pathology (United States) May 2004, 164 (5) p1727-37, ISSN 0002-9440 Journal Code: 0370502

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Phosphorylation of proteins on serine or threonine residues preceding proline (pSer/Thr-Pro) is a major regulatory mechanism in cell proliferation and transformation. Interestingly, the pSer/Thr-Pro motifs in proteins exist in two distinct cis and trans conformations, whose conversion rate is normally reduced on phosphorylation, but is catalyzed specifically by the prolyl isomerase **Pin1** . **Pin1** can catalytically induce conformational changes in proteins after phosphorylation, thereby having profound effects on catalytic activity, dephosphorylation, protein-protein interactions, subcellular location, and/or turnover of certain phosphorylated proteins. Recently, it has been shown that **Pin1** is overexpressed in human breast cancer cell lines and cancer tissues and plays a critical role in the transformation of mammary epithelial cells by activating multiple oncogenic pathways. Furthermore, **Pin1** expression is an excellent independent prognostic marker in prostate cancer. However, little is known about **Pin1** expression in other human normal and cancerous tissues. In the present study, we quantified **Pin1** expression in 2041 human tumor samples and 609 normal tissue samples as well as normal and transformed human cell lines. We found that **Pin1** was usually expressed at very low levels in most normal tissues and its expression was normally associated with cell proliferation, with high **Pin1** levels being found only in a few cell types. However, **Pin1** was strikingly overexpressed in many different human cancers. Most tumors (38 of 60 tumor types) have **Pin1** overexpression in more than 10% of the cases, as compared with the corresponding normal controls, which included prostate, lung, **ovary** , cervical, brain tumors, and melanoma. Consistent with these findings, **Pin1** expression in human cancer cell lines was also higher than that in the normal cell lines examined. These results indicate that **Pin1** overexpression is a prevalent and specific event in human cancers. Given previous findings that **Pin1** expression is an excellent prognostic marker in prostate cancer and that inhibition of **Pin1** can suppress transformed phenotypes and inhibit tumor cell growth, these findings may have important implications for the pathogenesis, diagnosis, and treatment of human cancers.

Prevalent overexpression of prolyl isomerase Pin1 **in human cancers.**

... conversion rate is normally reduced on phosphorylation, but is catalyzed specifically by the prolyl isomerase **Pin1** . **Pin1** can catalytically induce conformational changes in proteins after phosphorylation, thereby having profound effects on catalytic...

... subcellular location, and/or turnover of certain phosphorylated proteins. Recently, it has been shown that **Pin1** is overexpressed in human breast cancer cell lines and cancer tissues and plays a critical role in the transformation of mammary epithelial cells by activating multiple

oncogenic pathways. Furthermore, 1Pin1 expression is an excellent independent prognostic marker in prostate cancer. However, little is known about **Pin1** expression in other human normal and cancerous tissues. In the present study, we quantified **Pin1** expression in 2041 human tumor samples and 609 normal tissue samples as well as normal and transformed human cell lines. We found that **Pin1** was usually expressed at very low levels in most normal tissues and its expression was normally associated with cell proliferation, with high **Pin1** levels being found only in a few cell types. However, **Pin1** was strikingly overexpressed in many different human cancers. Most tumors (38 of 60 tumor types) have **Pin1** overexpression in more than 10% of the cases, as compared with the corresponding normal controls, which included prostate, lung, **ovary** , cervical, brain tumors, and melanoma. Consistent with these findings, **Pin1** expression in human cancer cell lines was also higher than that in the normal cell lines examined. These results indicate that **Pin1** overexpression is a prevalent and specific event in human cancers. Given previous findings that **Pin1** expression is an e

6252925 PMID: 15563182

Conformationally locked isostere of phosphoSer-cis-Pro inhibits Pin1 **23-fold better than phosphoSer-trans-Pro isostere.**

Wang Xiaodong J; Xu Bailing; Mullins Ashley B; Neiler Freda K; Etzkorn Felicia A

Department of Chemistry, Virginia Tech, Blacksburg, VA 24061-0212, USA.

Journal of the American Chemical Society (United States) Dec 1 2004, 126 (47) p15533-42, ISSN 0002-7863 Journal Code: 7503056

Contract/Grant No.: R01 GM 63271; GM; NIGMS; S10 RR 16658; RR; NCRR

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: In Process

Stereoisomeric cis and trans substrate analogues for **Pin1** were designed and synthesized. The central phosphoSer-Pro core of the **Pin1** substrate was replaced by cis and trans amide isosteres in Ac-Phe-Phe-pSer-Psi[(Z and E)CH=C]-Pro-Arg-NH(2), 1 and 2, peptidomimetics. They were synthesized on solid phase in 17% yield for the cis analogue 1, and 16% yield for the trans analogue 2. A second trans amide isostere with a C-terminal N-methylamide 3 was synthesized in 7% yield. The protease-coupled **Pin1** assay showed that all three compounds inhibited the **Pin1** peptidyl-prolyl isomerase (PPIase) enzymatic activity. The cis isostere 1 was 23 times more potent (K(i) = 1.74 +/- 0.08 muM) than its trans counterpart 2 (K(i) = 40 +/- 2 muM) in competitive inhibition of **Pin1** . These results suggest that the catalytic site of **Pin1** binds cis substrates more tightly in aqueous solution. Antiproliferative activity toward the A2780 human **ovarian** cancer cell line by the cis and trans analogues correlates with **Pin1** inhibition results.

Conformationally locked isostere of phosphoSer-cis-Pro inhibits Pin1 **23-fold better than phosphoSer-trans-Pro isostere.**

Stereoisomeric cis and trans substrate analogues for **Pin1**0 were designed and synthesized. The central phosphoSer-Pro core of the **Pin1** substrate was replaced by cis and trans amide isosteres in Ac-Phe-Phe-pSer-Psi...

... with a C-terminal N-methylamide 3 was synthesized in 7% yield. The protease-coupled **Pin1** assay showed that all three compounds inhibited the **Pin1** peptidyl-prolyl isomerase (PPIase) enzymatic activity. The cis isostere 1 was 23 times more potent...

... muM) than its trans counterpart 2 (K(i) = 40 +/- 2 muM) in competitive inhibition of **Pin1** . These results suggest that the catalytic site of **Pin1** binds cis substrates more tightly in aqueous solution. Antiproliferative activity toward the A2780 human **ovarian** cancer cell line by the cis and

STEM:OS - DIALOG OneSearch
File 155:MEDLINE(R) 1951-2005/Apr W3
(c) format only 2005 The Dialog Corp.
File 55:Biosis Previews(R) 1993-2005/Apr W3
(c) 2005 BIOSIS
File 34:SciSearch(R) Cited Ref Sci 1990-2005/Apr W3
(c) 2005 Inst for Sci Info
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
(c) 1998 Inst for Sci Info
File 340:CLAIMS(R)/US Patent 1950-05/Apr 21
(c) 2005 IFI/CLAIMS(R)
***File 340: 2004 Reload is online as of October 6, 2004. Pricing** changes effective October 1, 2004. See HELP NEWS 340 for details.

Set	Items	Description
? s pin1 or pin(w)1		
Processing		
Processing		
	693	PIN1
	190938	PIN
	13238761	1
	313	PIN(W)1
S1	981	PIN1 OR PIN(W)1
? s uterus or endometri? or ovar?		
	107805	UTERUS
	116900	ENDOMETRI?
	397870	OVAR?
S2	561947	UTERUS OR ENDOMETRI? OR OVAR?
? s s1 and s2		
	981	S1
	561947	S2
S3	27	S1 AND S2
? rd		
>>>Duplicate detection is not supported for File 340.		
>>>Records from unsupported files will be retained in the RD set.		
...completed examining records		
S4	21	RD (unique items)
? t s4/3,k,ab/1-21		

4/3,K,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 The Dialog Corp. All rts. reserv.

16252925 PMID: 15563182
Conformationally locked isostere of phosphoSer-cis-Pro inhibits Pin1 **23-fold better than phosphoSer-trans-Pro isostere.**
Wang Xiaodong J; Xu Bailing; Mullins Ashley B; Neiler Freda K; Etzkorn Felicia A
Department of Chemistry, Virginia Tech, Blacksburg, VA 24061-0212, USA.
Journal of the American Chemical Society (United States) Dec 1 2004, 126 (47) p15533-42, ISSN 0002-7863 Journal Code: 7503056
Contract/Grant No.: R01 GM 63271; GM; NIGMS; S10 RR 16658; RR; NCRR
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
Stereoisomeric cis and trans substrate analogues for **Pin1** were designed and synthesized. The central phosphoSer-Pro core of the **Pin1** substrate

was replaced by cis and trans amide isosteres in Ac-Phe-Phe-pSer-Psi[(Z and E)CH=C]-Pro-Arg-NH(2), 1 and 2, peptidomimetics. They were synthesized on solid phase in 17% yield for the cis analogue 1, and 16% yield for the trans analogue 2. A second trans amide isostere with a C-terminal N-methylamide 3 was synthesized in 7% yield. The protease-coupled **Pin1** assay showed that all three compounds inhibited the **Pin1** peptidyl-prolyl isomerase (PPIase) enzymatic activity. The cis isostere 1 was 23 times more potent (K(i) = 1.74 +/- 0.08 muM) than its trans counterpart 2 (K(i) = 40 +/- 2 muM) in

FI Publication Control No: 2002-0025521 IFI Chemical Acc No: 2002-0006993
Document Type: C

PIN1 **AS A MARKER FOR ABNORMAL CELL GROWTH; DETECTING DEFECTIVE PROLIFERATION IN MAMMALS; OBTAIN SAMPLE TISSUE, MONITOR CONCENTRATION OF CANCER MARKER PROTEIN, INCREASED CONCENTRATION INDICATES CANCER**

Inventors: Lu Kun Ping (US); Wulf Gerburg (US); Zhou Xiao Zhen (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000

Publication (No,Kind,Date), Applic (No,Date):
US 20020025521 A1 20020228 US 2000726464 20001129
Priority Applic(No,Date): US 2000726464 20001129
Provisional Applic(No,Date): US 60-167800 19991129

Abstract: Methods for the use of **Pin1** as a marker of abnormal cell growth are disclosed. In one embodiment, the method includes detecting a level of **Pin1** to stage an abnormal cell growth, such as breast or prostate cancer. In another embodiment, the method includes evaluating the efficacy of a treatment of an abnormal cell growth, such as cancer, by monitoring the levels of **Pin1** . In another embodiment, the method includes evaluating the extent of metastasis of abnormal cell growth, such as cancer. The levels of **Pin1** can be protein levels or nucleic acid levels.

PIN1 **AS A MARKER FOR ABNORMAL CELL GROWTH...**

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...a treatment of an abnormal cell growth, such as cancer, by monitoring the levels of **Pin1** . In another embodiment, the method includes evaluating the extent of metastasis of abnormal cell growth, such as cancer. The levels of **Pin1** can be protein levels or nucleic acid levels.

Exemplary Claim: ...A method of detecting abnormal cell growth in a mammal, comprising assessing the level of **Pin1** in a test sample from the mammal, wherein an elevation in the levels of **Pin1** is indicative of abnormal cell growth.

Non-exemplary Claims: 2. The method of claim 1, wherein the level of **Pin1** is a protein level...

...3. The method of claim 1, wherein the level of **Pin1** is a nucleic acid level...

...The method of claim 7, wherein the cancer selected from the group consisting of breast, **ovarian** , prostatic, cervical, skin, digestive track or testicular cancer...

...abnormal cell growth in a mammal, comprising the steps of: (a) detecting a level of **Pin1** in a test sample; and (b) comparing the level of **Pin1** in the test sample with a control level, and wherein a difference in the level of **Pin1** in the test sample is indicative of abnormal cell growth in the mammal...

...11. The method of claim 10, wherein the level of **Pin1** is a protein level...

...12. The method of claim 10, wherein the level of **Pin1** is a nucleic acid level...

...The method claim 13, wherein the cancer is selected from the group consisting of breast, **ovarian** , prostatic, cervical, skin, digestive track, lung, kidney, liver or testicular cancer mammal by assessing the level of **Pin1** protein in a test sample from the mammal, comprising the steps of: (a) contacting the test sample with an antibody having specificity for **Pin1** under conditions suitable for binding of the antibody to **Pin1** thereby resulting in the formation of a complex between the antibody and **Pin1** ; (b) detecting the complex between the antibody and **Pin1** ; and (c) comparing the amount of the complex in the test sample with an amount...

...control sample, wherein an elevation in the amount of the complex between the antibody and **Pin1** in the test sample compared to the complex in the control sample is indicative of...

...method of claim 19, wherein the cancer is selected from the group consisting of breast, **ovarian** , prostatic, cervical, skin, digestive track, lung, kidney, liver or testicular cancer...

...abnormal cell growth in a mammal, comprising the steps of: a) detecting a level of **Pin1** nucleic acid in a test sample; and b) comparing the level of **Pin1** in the test sample with a level of **Pin1** in a control sample, wherein an elevation in the level of **Pin1** in the test sample compared to the control sample is indicative of abnormal cell growth...

...method further comprises performing a polymerase chain reaction with oligonucleotide primers capable of amplifying the **Pin1** nucleic acid prior to detection...

...contacting a test sample obtained from the mammal with a nucleic acid probe to a **Pin1** nucleic acid; b) maintaining the test sample and the nucleic acid probe under conditions suitable...method of determining a stage of an abnormal cell growth, comprising assessing a level of **Pin1** in a test sample from a mammal...

...30. The method of claim 28, wherein the level of **Pin1** is a protein level...

...determining a stage of abnormal cell growth in a mammal by assessing the level of **Pin1** in a test sample from the mammal, comprising the steps of: contacting the test sample with an antibody having specificity for **Pin1** under conditions suitable for binding of the antibody to **Pin1** thereby resulting in the formation of a complex between the antibody and **Pin1** ; and comparing the amount of the complex in the test sample with an amount of...

...34. The method of claim 31, further comprising determining a ratio of the amount of **Pin1** bound to a **Pin1** antibody to an amount of a non-**Pin1** cellular protein selected from the group con